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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LIU, SAMUEL W	

ART UNIT	PAPER NUMBER
1653	5

DATE MAILED: 01/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/976,219	OR ET AL.	
	Examiner	Art Unit	
	Samuel W Liu	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *5-10 and 12-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

Claims 1-12 are pending and the following is applicable to the pending claims.

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-4 and 11, drawn to a cyclosporin peptide and a process of making, are classified in class 514, subclasses 2 and 11.

II. Claims 5-10, drawn to a method of making the cyclosporin and derivatives *via* an organic synthesis, are classified in class 530, subclass 333 and 335.

III. Claims 12-14, drawn to a method of treating inflammatory disease by Administering pharmaceutical composition comprising cyclosporin, are classified in class 514, subclass 2 and 11, class 424, subclass class 278.1, and class 604, subclass 19.

The inventions are distinct, each from the other because of the following reasons:

Invention II and Invention I are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case, as opposed to the claimed process (Claims 5-10), Leitner, E. *et al.* teach recombinant synthesis of cyclosporin peptides in which the peptides are synthesized by cyclosporin synthetase (see US Pat. No. 5827706). In addition, Billich A. *et al.* (*J. Biol. Chem.* (1987) 267, 17258-17259) teach that unusual amino acid residue, *e.g.*, L-norvaline, methyl-Leucine and other modified residues can be incorporated into cyclosporin structure by an

enzymatic synthesis in combination of chemically synthesized residues (see especially page 17259).

Invention I and Invention III are related as product and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the synthesized cyclosporin derivatives can be used as an inhibitor for permeability transition pore in mitochondria during apoptosis.

Inventions II and III are related as different and/or distinct methods, a method of making the cyclosporin and derivatives *via* synthesis, and a method of treating inflammatory disease using pharmaceutical composition comprising the cyclosporin. These two methods differ with respect to method steps, end-products, targets, and ingredients; therefore, each method is patentably distinct.

Additional Election Under 35 USC 121

Regardless of the elected group, applicant is required under 35 US 121 (1) to elect a single disclosed peptide to which claims are restricted; and (2) to list all claims readable thereon including those subsequently added.

If Group I is elected, applicant is required under 35 US 121 (1) to elect a Y chemical group from Claims 1 and 3; a cyclosporin derivative from Claim 4, since these organic groups are chemically different and none of them can be substituted one for other, and each cyclosporin derivative are both structurally and functionally different which are required different synthetic

procedure and modification and has different pharmacological efficacy toward therapeutic application.

If group III is elected, applicant is required under 35 US 121 (1) to elect a disease state from claim 13 because each disease state required different pathological mechanism, route of administering of pharmaceutical composition, treatment procedure and outcome of treatment. For example, mechanism for asthma, a disorder caused by airways in lungs are inflamed and swollen; muscles surrounding your airways, irritated by inflammation, tighten and constrict spontaneously; and membranes in airway linings secrete excess mucus, which results in narrowed airways and obstructed airflow that typically lead to coughing, wheezing and shortness of breath is different from the mechanism causing allergic rhinitis, an immune disorder involving the antibody immunoglobulin E, or IgE. Therefore, methods of treatment for both diseases are different.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art shown by their different classification, art recognized divergent subject matter, separate search, restriction for examination purposes as indicated is proper.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art shown by their different classification, art recognized divergent subject matter, separate search, restriction for examination purposes as indicated is proper.

During a telephone conversation with Jason D. Ferrone on 3 January 2003 a provisional election was made with traverse to prosecute the Group I, Claims 1-4 and 11, and the subgroups "B" as -α-amino butyric acid, "U" as –(D) alanine, "X' as absent and "Y" as (2'-Br)Ph. Affirmation of this election must be made by applicants in replying to this Office action. Claims

5-10 and 10-14 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Thus, Claims 1-4 and 11 are pending and examined in this Office action.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Specification/Claim Objections

The disclosure is objected to because of the following informalities:

(1) The abstract of the current application exceeds 150 words in length. The abstract of the disclosure is objected to because the abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. A single paragraph of 150 words or less commencing on a separate sheet following the claims is required. See MPEP § 608.01(b). The language should be clear and concise.

(2) In page 7, line 36 "NFA" should be spelled out in full for the first instance of use. See also, page 8, line 5, "HIV"; page 9, line 2, "COPD"; page 10, line 26, "HCMV"; page, line 13, "HSP70"; page 29, line 2, "DMSO"; page 31, line 7, "MAP" kinase; page 31, line 31 "CHO";

page 31, line 35, "PMA"; page 32, line 21, "CBA" and line 27, "OFI"; and page 34, line 10, "HEPES" and line 14, "HBSS".

Appropriate correction is required.

Claim Rejections - 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Bollinger, P. *et al.* (EP 0296122).

Bollinger *et al.* disclose a cyclosporin structure that meets the limitations of the Formula (I) structure of claim 1 of the instant application (see page 5 formula (II) wherein "B" is αAbu, "X" is Sar, "Y" is Val, and "A" is set forth in formula (XIX) at page 19 wherein "R_6" group has the meaning given for formula (V) (see the second line, page 20), wherein formula (V) describes that "R_6" group is phenyl). Note that the reference patent is applied to "A2" moiety. Because Applicant elects "B" as -α-amino butyric acid, "U" as –(D) alanine, "X' as absent, and "Y" as (2'-Br)Ph for patent examination, and because Bollinger's patent also teaches that the phenyl group is further subject to Halogen substitution (see lines 35-37, page 8), claims 2-4 are anticipated by the patent reference as well.

In addition, Bollinger *et al.* teach a pharmaceutical composition comprising the disclosed cyclosporin analog and ingredient for formulation of the composition (see lines 38-64, page 33, and lines 13-50, page 34), as applied to claim 11 of the current application.

Provisional Rejection - Obviousness Type Double Patenting

Claims 1-3 and 11 of this application conflict with Claims 1-3 and 9 of Application No. 09975923 and claims 1-3 and 8 Application No. 09800856. 37 CFR 1.78(b) provides that when two or more applications filed by the same applicant contain conflicting claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their retention during pendency in more than one application. Applicant is required to either cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP § 822.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this

application. See 37 CFR 1.130 (b). Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3 and 11 are provisionally rejected under the judicially created doctrine of double patenting over claims 1-3 and 9 of copending Application No. 09975293. This is a provisional double patenting rejection because the conflicting claims have not in fact been patented.

Claim 1 of Application 09975923 [see formula I] discloses a cyclosporin analog that is an obvious structural variation of that set forth in the claim 1 [formula (A1)] of the current application. In formula (I) of 09975923, moiety of "A" is an obvious structural variation over the moiety of "A" set forth in formula (I) of the present application in that, provided that "Y" is a functional group, *e.g.*, aryl, and "X" is absent, moiety "B" and "U" are identical for Application 09975923 and the current application.

Claim 2 of Application 09975923 and claim 2 of the present application is identical.

Claim 3 of Application 09975923 and claim 3 of the present application disclose the common subject matter but with different scope with regard to "Y" moiety.

Claim 9 of Application 09975923 and claim 11 of the instant application are identical.

Therefore, the instant application and copending application claims are obvious variation. The claims of the present application are not patentably distinct from the claims of Application 09975923.

Claims 1-3 and 11 are provisionally rejected under the judicially created doctrine of double patenting over claims 1-3 and 8 of copending Application No. 09800856. This is a provisional double patenting rejection because the conflicting claims have not in fact been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows:

Claim 1 of Application 09800856 [see formula I] discloses a cyclosporin analog that is an obvious structural variation of that set forth in the claim 1 [see formula (1)] of the current application. In formula I of 09800856, moiety of "A" is the same as moiety of "A1" set forth in formula (1) of the present application in that, provided that "Y" is a functional group, *i.e.*, aryl, "X" is absent, moiety "B" and moiety "U" are identical for Application 09800856 and the current application.

Claims 2-3 of the Application 09800856 and claims 2-3 of the current application disclose the common subject matter but with different scope in regard to the "Y" moiety.

Claim 8 of the Application 09800856 and claim 11 of the current application set forth the common subject matter as to a pharmaceutical composition comprising a cyclosporin compound or/and a pharmaceutically acceptable carrier.

Therefore, the instant application and copending application claims are obvious variation. The claims of the present application are not patentably distinct from the claims of Application 09800856.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Wei Liu whose telephone number is (703) 306-3483. The examiner can normally be reached from 9:00 a.m. to 5:00 p.m. on weekdays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Christopher Low, can be reached on 703 308-2923. The fax phone number for the organization where this application or proceeding is assigned is 703 308-4242 or 703 872-9306 (official) or 703 872-9307 (after final). Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 305-4700.

Samuel Wei Liu

January 14, 2003

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